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New developments in funding the life sciences to make research more effective

Funding for the life sciences, in particular for biomedical research, has increased enormously during the past few decades. The budget for the US National Institutes of Health (Bethesda, MD, USA) alone nearly quadrupled from US$7.5 billion in 1990 to US$28.5 billion in 2006. Although this might be an extreme example, the overall trend is clear: biomedical research, both fundamental and applied, receives an enormous amount of publicly financed funding—and not just in the USA. Citizens and politicians all over the world hope that research will deliver new cures, therapies and diagnostics for a wide range of diseases.

However, there is growing concern among stakeholders—ultimately patients and taxpayers—that they are not getting value for money. The ‘war against cancer’, declared as early as 1971, is far from being won, and similar wars against Parkinson disease and Alzheimer disease are also not going well. These and other failures have caused many Europeans, among others, to think about more efficient funding mechanisms—sometimes based on proven practices in other areas such as finance, electronics and information technology. Of course, there are also some examples of successful funding strategies within the life sciences, such as the contributions of one prominent financier to research into prostate cancer during the 1990s—but these tend to be the exceptions.

Inevitably, the decision to fund research rests on the question of how to measure a return on investment. The problem is that payback can be assessed in different ways—for example, a cure is found, a vaccine is brought a step nearer, patents are won—and often takes years to materialize. But even without clear guidelines for measuring success, research in many biomedical fields, notably those focusing on certain cancers and some infectious diseases, has not gone well. Despite ever growing levels of funding, research has not yielded many new treatments; only some patchy progress in reducing mortality levels.

This came as a surprise to cancer survivor and business journalist Clifton Leaf, who resigned as executive editor of Fortune Magazine in March 2007. He is now writing a book about the war on cancer to be published early in 2008—a follow-up to a cover story in Fortune Magazine (Leaf, 2004). Leaf initially started his research with the expectation of reporting progress. “I thought that this was the future, the brave new world of molecularly targeted medicines,” he said, “but instead I discovered a system in complete dysfunction. My preconceived notion was the opposite of where I ended up.”

Leaf then became a figurehead calling for a reform in the way cancer research is conducted and funded. According to his analysis, one problem is a generally narrow research focus, with too much emphasis placed on reductionist approaches that study specific markers or biochemical reactions in animal models. “That gets us thinking smaller and smaller, and sometimes leads to great discoveries. But
sometimes there's more to the picture than anatomical mechanistic processes,” he said. But Leaf also heaped blame on the grant-making process for retarding progress. “I’ve never met anyone who would tell you this is a terrific way of figuring out how science ought to be done,” he said, pointing out that the current grants system is not only consuming too much intellectual effort, but also distorting the whole shape and focus of projects.

This is a common sentiment among researchers. The UK pioneer of systems biology, Denis Noble, at Oxford University, UK—who developed the first computer simulation of the human heart in 1960—agreed that the increase in funding had been a mixed blessing. “The funding available is much larger than 40 years ago, but the administrative burden of getting it and managing it has become counterproductive,” he commented. “A sure sign that the admin burden is too large is that teams have to have specialist admin people, particularly to secure and administrate EU funding.”

This not only distracts scientists from their work, but can also alter the direction of research—as noted by Bruce Charlton, an evolutionary psychiatrist at the University of Newcastle upon Tyne in the UK, and a critic of the current funding process for medical science. Charlton has argued that scientists are being forced to dress up fundamental work with claims of potential applications or cures. “Normal science is being marketed by spin doctors as if it were revolutionary science,” he said. However, in reality, most basic research in medicine involves extrapolation of existing theories and precise checking of previous results. “Yet this administrative work is presented as if it were radical, and paradigm-shifting science, and the project managers presented as if they are the heirs to Crick and Watson,” Charlton added.

This leads to another problem, in Charlton’s opinion: too much emphasis is placed on using large-scale ‘basic-to-applied’ integrated programmes to tackle every step of research, from invention or discovery through to therapy. Although this focus on ‘big science’ might be distorting fundamental research, there is an obvious need for clear end goals, especially in medical science. “I believe that a substantial part of funding should be directed to achievable practical goals,” agreed Noble. “Systems biology, for example, is vast, and funders will lose patience if, after 10 years, there is little benefit to show.”

Most worryingly, Charlton has argued that disillusionment might start to kick in and that medicine is in danger of following the same trajectory as twentieth century physics. Large increases in funding for physics research followed a string of breakthroughs by scientists such as Albert Einstein and Werner Heisenberg, only for the investment bubble to burst when the breakthroughs dried up in the middle of the century. Since then, the life sciences have taken over as the source of important discoveries.

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arlton’s plan for keeping funders onboard while motivating scientists to do practical research that yields real benefits is to offer massive prizes (Charlton, 2007). This, he argued, would provide the incentive to pursue solutions that might work even in stagnant fields of research. This is in contrast to grants, which tend to encourage pure science, or patents, which favour only new technologies. Charlton has subsequently urged medical charities to accumulate or even pool their resources until they can offer a prize big enough—perhaps worth tens of millions of dollars or more—to solve a problem on behalf of the patients that they represent.

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Such mega-projects, focusing on a particular problem or disease, have often been funded at a national level within Europe—either by health services or by research councils. Sometimes this results in an uneasy split between the two because the councils focus on long-term strategic research, whereas health services have to cater to patients and administer hospitals. In the UK, for example, the Medical Research Council (MRC; London, UK) has a mission to fund research that might not appeal to the private sector. “We will support things companies cannot afford, perhaps where a drug out of patent finds new uses,” explained George Sama, Assistant Director of Strategy at the MRC. Examples include aspirin, the anti-thrombotic effects of which make it valuable for treating heart disease and strokes, and folic acid, which is used to treat many conditions including anaemia. But, Sama added, “there are also treatments and procedures like cognitive and behavioural therapies that again may not have a commercial market and yet can be very effective.”

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However, medical research in the UK is also funded directly by the Department of Health—a split that can lead to the fragmentation of important research and a failure to tackle the big questions. According to Peter Cotgreave, Chief Executive of the lobbying group, the Save British Science Society (London, UK), “The NHS research budget has not been used in a strong powerful way to answer those big questions […] The government gave the NHS new money specifically for cancer research a few years ago, and when the select committee [a parliamentary monitoring group] examined where it had gone, it hadn’t gone into research at all.” Instead it had gone into the administrative pot. According to Sama, an attempt to harmonize UK public funding is now being made by merging the funds of the MRC and the Department of Health.

The Netherlands has already implemented this kind of solution after concluding that the conflicts of interest between the research council and ministry of health were insurmountable. John Marks, former director of the Earth and Life Sciences division of the Netherlands Organisation for Scientific Research (NWO; Den Haag), and recently appointed CEO of the European Science Foundation (ESF; Strasbourg, France), said, “In the Netherlands, we have made that transition whereby the Ministry of Health transferred its funding for translational research [exploiting basic research in new drugs and therapies] and testing new treatments to the NWO funding agency 10 years ago.”
Marks believes that this move has helped to distribute funding more effectively and equitably across all components of the research and development pipeline. “What is important is that in the design of research programmes, you actually involve all communities from the very beginning and don’t distinguish between Blue Skies, basic research, applications, and new treatments,” he said. With all partners involved in design, it is easier to identify at the outset what the principle questions are, and then decide where best to conduct each component of research. “Some of these questions require research more in the university atmosphere, while others are closely linked to hospitals, and yet others are more suitable for the pharmaceutical companies,” Marks added.

However, this goal-oriented approach is not conducive to pure, basic research, which in the past has led to significant discoveries—such as monoclonal antibodies—that only later turn out to have a therapeutic use. Therefore, Noble thinks that a separate mechanism is required to stimulate fundamental research and to ensure that there is the right emphasis on it. “It is important also to fund the people who are genuinely innovative to go where their instinct leads them. I think a system of research points would be valuable. After accumulating sufficient track record points, a leader should be free to take some risks,” he said.

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But even this approach might not help scientists whose immediate objective is to gain a deeper understanding of fundamental biological processes—unless research points are scored purely on the basis of merit, publication or citation. Jim Barber, at Imperial College London, UK, is one of the world leaders in the study of photosynthesis and has helped to elucidate the water-splitting mechanism of the catalytic core (Ferreira et al, 2004). However, Barber is now unsure whether he will be able to continue his research, even though it is playing a crucial role in the emerging field of solar energy conversion, which could provide carbon-neutral energy in the future. “My modest grant comes to an end this August and if the Biotechnology and Biological Sciences Research Council [BBSRC; London, UK] application I have just submitted fails then that’s the end of it,” he said. “I feel very concerned about how to maintain the expertise we have established over the years which makes us a major international player.”

Charlton agreed that Europe as a whole needs to encourage more pure science of this kind, “since there is very little top revolutionary science in Europe now—or anywhere outside the USA.”

The European Union has accepted this deficiency and has responded by setting up the European Research Council (ERC; Brussels, Belgium), with a focus on ground-breaking science. “I think that the recent launch of the ERC will make a significant contribution to stimulating revolutionary research in Europe, as it will be supporting science based on excellence alone,” said Fiona Kernan, scientific officer at the ESF.

Meanwhile, Europe is also tackling the issue of funding large integrated projects through its Eurobiofund as part of the ESF. This is a bold attempt to create a marketplace where funders and scientists can meet to assemble budgets that are sufficient for large projects. The big challenge, according to the Eurobiofund director, Wouter Spek, lies in persuading several funding parties with different interests that they will all benefit from contributing to a given project. He believes that part of the answer lies in applying sound financial principles to financing science: “I think I call it financial engineering. We need to look at how we can make use of normal financial activities to invest in research,” he said.

Eurobiofund is also studying how research is funded in other fields, such as electronics, in which small companies have a much bigger role in innovation than in biotechnology at present. However, there have also been successes in big-budget biomedical research that Eurobiofund should consider—for example, in the case of prostate cancer. This became an important story in the USA during the 1990s when Michael Milken founded the Prostate Cancer Foundation (Santa Monica, CA, USA) in 1993, after being released from a prison sentence for insider trading. Having made his fortune from the junk bond market in the 1980s, he developed prostate cancer in the early 1990s and applied his renowned energies to finding a cure.

Milken and many others survived because of the changes made to treatment brought about by the Prostate Cancer Foundation. Leaf noted, “we don’t quite know how it happened, probably for a lot of reasons.” There was better screening and more effort put into the field as a whole, with greater willingness to try different treatments, sometimes in combination, Leaf added. But he also conceded that many early successes in treating cancer sprang from a more lax regulatory environment, which allowed for the testing of a wider variety of drugs. “If you look at the early history, success came from trying out lots of drugs in combination, often with horrific results,” he said.

The question then, is how to replicate early successes without taking unacceptable risks with patients. The answer lies in obtaining the right human tissue. “The complete lack of an infrastructure for human tissue is one of the most aggravating mysteries one could imagine,” Leaf said. There are some attempts through biobanking initiatives, but at present it is practically impossible for many researchers to get the tissue they need, even when it almost certainly exists in a laboratory or cold room somewhere not far away. As a possible solution, Leaf pointed to Estonia as a shining example of a country that has established a highly successful and operational national biobank without massive funding.

But not all is in tatters in biomedical research: there are many good examples and good practices where money has been spent effectively for life science research. However, as Charlton and others believe, it might also be a sign that a long period of ever expanding and unchecked funding for the life sciences is coming to an end. With the higher expectations of patients and taxpayers, researchers might have to get used to doing more goal-oriented research or operating within an arena of contracting budgets. It might well be possible to win the war against cancer and other diseases—but the arsenal and the money to pay for it must be used more wisely.

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